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Size Specific Trapping at a Convergent Stagnation Point

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DNA has been observed to be trapped at a convergent stagnation point created by opposite rotating vortices in simulations based on the lattice-Boltzmann method using a bead-spring model for the DNA. Previous work has successfully separated polymers whose length differs by a factor of 2. However more precise separation based on length could potentially be achieved. Preliminary simulations have trapped 60% of the smaller strands in polymers length ratio 1.5:1. Mastering this technique could allow advancements in developing microfluidic techniques for DNA amplification based on PCR and purification of the PCR product. Additionally these simulations mimic conditions found in pores of hydrothermal vents, giving hypothesis on the development of life.

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The Physical Foundation of Vaso-Occlusion in Sickle Cell Disease

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The pathology of sickle cell disease arises from the occlusion of small blood vessels because of polymerization of the sickle hemoglobin within the red cells. We present measurements using a novel microfluidic method to determine the pressure required to eject individual red cells from a capillary-sized channel after the cell has sickled. We find that the maximum pressure is only around 100 Pa, much smaller than typically found in the microcirculation. This explains why experiments using animal models have not observed occlusion beginning in capillaries. The magnitude of the pressure and its dependence on intracellular concentration are both well described as consequences of sickle hemoglobin polymerization acting as a Brownian ratchet. Given the recently-determined stiffness of sickle hemoglobin gels (Zakharov, Aprelev, Turner & Ferrone, Biophys J, 99:1149-1156, 2010), the observed obstruction seen in sickle cell disease as mediated by adherent cells can now be rationalized, and surprisingly suggests a window of maximum vulnerability to occlusion during the circulation of sickle cells.

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Engineering Myosin V Velocity by Tuning Nanocomposite Morphology

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Devices which utilize biological components such as molecular motors may be capable of detecting or separating analytes with speed and resolution rivaling macroscopic instruments. The design and manufacturing of such devices requires detailed understanding of self-assembly and interactions of biological materials with synthetic environments. We demonstrated that nano-scale roughness modulates surface binding of F-actin (Langmuir 28:12216; 2012). By controllably converting a thin film of polystyrene-random-tert butyl acrylate copolymer to polyacrylic acid (PAA), we grafted amine-functionalized nanoparticles at high coverage to the PAA hydrogel, creating a surface with tunable roughness. Extending that approach here, we explore the effect of nanocomposite morphology on myosin V processive motility. We find that tuning the size and density of the surface grafted nanoparticles controls the velocity and run length of myosin V. Velocity decreases significantly as the nanoparticle size is increased independent of the concentration of MgATP. This effect of particle size may be due to changes in net charge, nanoparticle curvature at the interaction sites, or tortuosity of the actin imposed by the surface features. Experiments to distinguish these hypotheses are underway. Further understanding of the relationship between nanoparticle surface morphology and activity of actin in support of motility may permit the engineering of stops or stalls with high spacial precision into biomolecular devices. Supported by NSF/NSEC grant DMR08-32802.

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Time Dependent effects of Engineered Nanoparticles on the Biophysical Function of a Model Lung Surfactant

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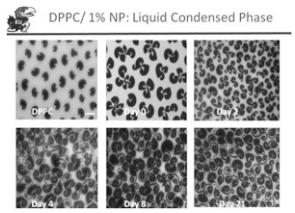
Increased manufacturing of engineered nanoparticles (ENPs) with commercial and biomedical applications has led to an increase in the release of these particles into the environment. Since the pulmonary route is an obvious one for the intake of these nanoparticles, concerns regarding potential health risks of these NPs has also seen a rapid increase in recent years.

In this work, we describe the interaction of an engineered carbon nanoparticle (nanodiamond ENDs) with a model lung surfactant system (DPPC) both as a function of time of exposure and concentration. Using surface pressure vs. area per molecule coupled with fluorescence microscopy, we study lipid/END interactions for several weeks. Our results indicate that over short times (0-2 days exposure) the ENDs do not significantly affect the biophysical properties of this model surfactant. However after longer exposure, the ENDs begin to alter the surface tension lowering ability and domain morphology of DPPC. Our results indicate that long term exposure to these ENDs cause a lowering of line tension of the film, in a manner similar to interactions between DPPC and small (<2 wt %) amounts of cholesterol.



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Interfacial Activity of Pulmonary Surfactant Combined with Gold Nanoparticles: A Promising Tool in Lung Medicine

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Lungs epithelium is the largest surface of the human body in contact with the environment to provide the needed gas exchange for living. It is covered by Pulmonary Surfactant (PS), which is a lipid-protein complex in charge of reducing the surface tension at the air-liquid respiratory interface so minimizing the work of breathing. Thereby, collapse is avoided. Likewise PS is responsible for innate defense mechanisms preventing the entry of inhaled pathogenic entities.

As a result of this lung specific design, the pulmonary route of administration is acquiring a large projection in the design of new strategies in medicine. It offers a great number of benefits in local treatment of lung diseases. In this context, Gold Nanoparticles (GNPs) seem to be a promising tool. They might improve current diagnostics and treatments due to their outstanding optical properties and ease of tuning size and shape.

Since the PS layer is the first surface where NPs impinge, many studies are analyzing the influence of NPs onto the biophysical properties of PS, which will define their distribution and clearance. Therefore a deep understanding of NP-PS interaction is required as a previous step to elucidate their impact on toxicity and to develop the potential of PS as an efficient and selective vehicle of NPs. The aim of this work is to analyze the size and coating effect of GNPs, on the functional properties of native PS purified from porcine broncholveolar lavage. The interfacial activity of PS/NP combinations has been assessed by captive bubble surfactometry and surface balances. The results suggest that it is quite feasible to design GNP-PS complexes with suitable features to being used in real clinical settings.

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Targeting of Melanoma by pH (Low) Insertion Peptide (pHLIP)

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pH (low) insertion peptide (pHLIP) is a helical peptide capable of inserting itself across a cell membrane at low pHs, but not at normal physiologic pH. It possesses two carboxyl groups on aspartic acid residues in its transmembrane region which are protonated at low pH, thereby increasing the peptide's hydrophobicity and facilitating transmembrane insertion. As a result, pHLIP can be used to specifically target acidic disease tissues, including solid tumors, in vivo. Here, intravenously injected fluorescent-labeled pHLIP is shown to localize to melanoma in two different genetically engineered mouse models. These mouse models harbor melanocyte-specific conditional alleles for mutations commonly present in melanoma. Upon activation of the mutations by topical 4-hydroxytamoxifen administration, these mice develop tumors from endogenous melanocytes, thereby closely recapitulating the development of tumors in a natural environment (Dankort et al., Nature Genetics 41, 544-52 (2009); Damsky et al., Cancer Cell 20, 741-54 (2011)). To date, this is the most realistic tumor model in which pHLIP has been utilized, and our results demonstrate for the first time that pHLIP is capable of localizing to cutaneous lesions. This opens the possibility of utilizing pHLIP for the detection of melanoma and other skin cancers. In addition, pHLIP is capable of translocating polar molecules attached to its inserting end across cell membranes. Currently, we are taking advantage of this property in order to develop pHLIP-based therapies against melanoma.